Remarks

Claims 1, 3, 5, 7, 9, and 11-64 are in this application. Claims 1, 3 and 11 have been amended. Claims 2, 4, 6, 8, 10 and 65 have been canceled. The subject matter of claim 2 has been incorporated into claim 1 and the subject matter of claim 4 has been incorporated into claim 3.

The title of the application has been amended to "Pharmaceutically acceptable salts of Phenoxazine and Phenothiazine compounds."

The first page of the specification has been amended to include the statement "This application claims the benefit of U.S. Provisional application 60/267,235 filed on February 5, 2001."

The Examiner rejected claims 1-10 and 12-65 under 35 USC 112, second paragraph. Applicants respectfully traverse this rejection.

Claims 1 and 3 have been amended to delete the phrase "its derivatives, its analogs."

Therefore, it is respectfully requested that this rejection be withdrawn.

The Examiner has rejected claims 30-35 and 52-55 stating that there is no antecedent basis in claim 24. Applicants respectfully traverse this rejection.

There is a relationship between insulin resistance and inflammation. The anti-inflammatory effects of glitazones, a major class of drugs which decrease insulin resistance, have been demonstrated by preventing atherosclerotic lesions. In Ishibashi et al., Hypertension 2002 Nov.; 40 (5): 687-93 the anti-inflammatory effect of pioglitazone on coronary inflammation mediated by chronic administration of L-NAME (N (omega)-nitro-L-arginine methyl ester), an endothelial NO synthesis inhibitor was shown. Similar effects have been observed

for other thiazolidinediones such as rosiglitazone and troglitazone (See Dandona, P. Curr. Diab. Rep. 2002 Aug; 2(4): 311-5.

Kidney Int 2001 Jul;60(1): 14-30 discloses .

Peroxisome proliferator-activated receptors (PPARs): Novel therapeutic targets in renal disease. Peroxisome proliferator activated receptors (PPARs) are members of the nuclear hormone receptor superfamily of ligand-dependent transcription factors. PPARs play an important role in the general transcriptional control of numerous cellular processes, including lipid metabolism, glucose homeostasis, cell cycle progression, cell differentiation, inflammation and extracellular matrix remodeling. PPARalpha primary regulates lipid metabolism and modulates inflammation. PPARalpha is the molecular target of the hypolipidemic fibrates including bezafibrate and clofibrate. PPARgamma is a key factor in adipogenesis and also plays an important role in insulin sensitivity, cell cycle regulation and cell differentiation. Antidiabetic thiazolidinediones (TXDs) such as troglitazone and rosiglitazone are specific ligands of PPARgamma, and this interaction is responsible for the insulin-sensitizing and hypoglycemic effect of these drugs. The kidney has been shown to differentially express all PPAR isoforms. PPARalpha is predominantly expressed in proximal tubules and medullary thick ascending limbs, while PPARgamma is expressed in medullary collecting ducts, pelvic urothelium and glomerular mesangial cells. PPARbeta is ubiquitously expressed at low levels in all segments of nephron. Accumulating data has begun to emerge suggesting physiological and pathophysiological roles of PPARs in several tissues including the kidney. The availability of PPAR-selective agonists and antagonists may provide a new approach to modulate the renal response to diseases including glomerulonephritis, glomerulosclerosis and diabetic nephropathy.

Dubuquoy L., et al. "Peroxisome proliferator-activated receptor (PPAR)

gamma: a new target for the treatment of inflammatory bowel disease", Gastroenterol. Clin. Biol. 2000 Aug-Sept. 24(8-9), 719-24 discusses that PPARgamma agonists may have therapeutic utility in inflammatory bowel diseases.

The following references support that the use of the claimed compounds in treating Alzheimer's disease.

Messier, C. et. al, "Glucose regulation and cognitive functions: relation to Alzheimer's disease and diabetes", Behavioural Brain Research 75(1996) 1-11 discusses the relationship between altered glucoregulation and Alzheimer's disease.

Hull, M., "Pathways of inflammatory activation in Alzheimer's disease: potential targets for disease modifying drugs", Curr. Med. Chem. 2002 Jan. 9 (1):83-8 discusses that PPAR gamma agonists may be suitable agents to suppress inflammatory activation in Alzheimer's disease.

See also Watson, G.S. et al. "The role of insulin resistance in the pathogenesis of Alzheimer's disease: implications for treatment." CNS Drugs 2003; 17(1) 27-45.

The following references support the use of the claimed compounds for preventing and treating cancer.

Kopelovich, L. et al. , "Peroxisome proliferator-activated receptor modulators as potential chemopreventative agents", Mol. Cancer. Ther. 2002 Mar. 1(5):357-63. ("This review presents a rationale for using PPAR modulators as cancer chemopreventative drugs.)

Pershadsingh, H. "Pharmacological peroxisome proliferator-activated receptor ligands:emerging clinical indications beyond diabetes" Expert. Opin.

Invest. Drugs 8(11), 1859-1872 discusses the use of PPAR gamma ligands in the treatment of carcinogenesis.

Therefore, it is respectfully requested that this rejection be withdrawn.

The Examiner has rejected claims 20-23 under 35 USC 112, first paragraph as not being enabled. Applicants respectfully traverse this rejection.

In view of the submission of the Kopelovich and Pershadsingh references, the disclosure in this application and the knowledge of one skill in the art it is respectfully requested that this rejection be withdrawn.

The Examiner has rejected claims 30-35 and 52-55 under 35 USC 112, first paragraph on the as not being enabled. Applicants respectfully traverse this rejection.

In view of the submission of the references listed above which describe the mechanisms and/or prevention and/or treatment of Alzheimer's disease, inflammation and cancer, the disclosure in this application and the knowledge of one skill in the art it is clear that one of skill in the art would be able to make and use the invention. Therefore, the enablement requirement is met.

It is respectfully requested that this rejection be withdrawn.

The Examiner rejected claims 1, 3, 5, 7, 12, 16, 20, 24, 26, 30, 36, 38, 42, 44, 64 and 65 as being anticipated under 35 USC 102(e) as being anticipated by US patent 6,054,453. Applicants respectfully traverse this rejection.

Applicants respectfully state that the rejection under 35 USC 102(e) is improper.

Claim 1 has been amended to include the subject matter of claim 2 and claim 3 has been amended to include the subject matter of claim 4. Therefore, this rejection is moot.

The Examiner rejected claims 1, 3, 5, 7, 12, 16, 20, 24, 26, 30, 36, 38, 42, 44, 64 and 65 under 35 USC 102(b) as being anticipated by Lohray (WO99/19313). Applicants respectfully traverse this rejection.

Claim 1 has been amended to include the subject matter of claim 2 and claim 3 has been amended to include the subject matter of claim 4. Therefore, this rejection is moot.

The Examiner rejected claims 1-10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64 and 65 under 35 USC 102(e) as being anticipated by Lohray (US patent 6,440,961). Applicants respectfully traverse this rejection.

Applicants respectfully state that the rejection under 35 USC 102(e) is improper.

Claim 1 has been amended to include the subject matter of claim 2 and claim 3 has been amended to include the subject matter of claim 4. Therefore, this rejection is moot.

The Examiner rejected claims 1-10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64 and 65 under 35 USC 102(e) as being anticipated by WO 00/50414. Applicants respectfully traverse this rejection.

Applicants respectfully state that the rejection under 35 USC 102(e) is improper.

Claim 1 has been amended to include the subject matter of claim 2 and claim 3 has been amended to include the subject matter of claim 4. Therefore, this rejection is moot.

The Examiner has rejected claims 1-10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64 and 65 under 35 USC 102(f) as being anticipated by US Patents 6,054,453 and 6,440,961. Applicants respectfully traverse this rejection.

Applicants respectfully state that the rejection under 35 USC 102(f) is improper.

Claim 1 has been amended to include the subject matter of claim 2 and claim 3 has been amended to include the subject matter of claim 4. Therefore, this rejection is moot.

The Examiner has rejected claims 1, 12, 16, 20, 24, 26, 30, 42 and 44 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12, 17 and 18-42 over US Patent 6,054,453. Applicants respectfully traverse this rejection.

In view of the amendment of claims 1 and 3, applicants submit that this rejection is moot and respectfully request that the rejection be withdrawn.

The Examiner has rejected claims 1, 2, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60 and 62 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14, 19, 21-67 and 69-77 over US Patent 6,440,691. Applicants respectfully traverse this rejection.

In view of the amendment of claims 1 and 3, applicants submit that this

rejection is moot and respectfully request that the rejection be withdrawn.

The Examiner states that claims 1, 2, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60 and 62 are directed to an invention not patentably distinct from claims 1-14, 19, 21-67 and 69-77 of commonly assigned U.S. Patent 6,440,961. Applicants respectfully traverse this rejection.

For the reasons stated above, claims 1, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60 and 62 are patentably distinct from the claims of US Patent 6,440,961.

Pursuant to 37 CFR 1.78(c), applicants state that the inventions of US patent application 10/067,096 and US patent 6,440,961 were commonly owned at the time the invention in this application was made.

The Examiner provisionally rejected claims 1, 12, 16, 20, 24, 26, 30, 32, 36, 38, 42 and 44 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-30 of copending application no. 10/007,109. Applicants respectfully traverse this rejection.

It is respectfully requested that the provisional obviousness-type patent rejection over US patent application 10/007,109 be withdrawn. A preliminary amendment was filed with this application on November 9, 2001 in which claims 1-33 were cancelled and claim 34 was added. A copy of the preliminary amendment and the postcard date stamped by the US Patent and Trademark Office is attached. Since none of the claims in this application are obvious over claim 34 of US patent application 10/007,109, it is respectfully requested that this rejection be withdrawn.

Accordingly, applicants submit that the present application is in condition for allowance and favorable consideration is respectfully requested.

Respectfully submitted,

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